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FAX COVER SHEET

	NAME	COMPANY NAME	TELECOPY NO.
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FROM: Jill T. Powlick

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Faxed: December 29, 2003
Applicant: Carl T. Wittwer
Invention: AUTOMATED ANALYSIS OF REAL-TIME NUCLEIC ACID AMPLIFICATION
Serial No.: 10/074,169
Filed: February 12, 2002
Docket: 7475-70049

X Response to Restriction Requirement (5 pages)

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group:	1655
Confirmation No.:	5884
Application No.:	10/074,169
Invention:	AUTOMATED ANALYSIS OF REAL-TIME NUCLEIC ACID AMPLIFICATION
Applicant:	Carl T. Wittwer
Filed:	February 12, 2002
Attorney Docket:	7475-70049
Examiner:	Fredman

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on December 29, 2003

Joyce Hamilton
(Signature)

Joyce Hamilton
(Printed Name)

Response to Restriction Requirement

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed on November 28, 2003, the Applicant respectfully requests entry of the following amendments and consideration of the following remarks. The Applicant believes that no additional fees are required with this response. If fees are required, it is respectfully requested that the fees be charged to the account of Barnes & Thornburg, Deposit Account No. 10-0435, with reference to our matter 7475-70049.

IN THE CLAIMS:

1. (original) A method for determining the presence of a nucleic acid in a sample comprising the steps of

providing a fluorescent entity capable of indicating the presence of the nucleic acid and capable of providing a signal related to the quantity of the nucleic acid,

amplifying the nucleic acid through a plurality of amplification cycles in the presence of the fluorescent entity,

measuring fluorescence intensity of the fluorescent entity at each of the plurality of amplification cycles to produce a fluorescent value for each cycle related to the quantity of the nucleic acid present at each cycle,

generating a plot wherein the fluorescent values are recorded for each amplification cycle,

performing a confidence band analysis on the plot to generate a positive or negative call, and

if the call is positive, confirming the positive call by a melting temperature analysis.

2. (original) The method of claim 1 wherein the confidence band analysis is performed by

calculating slopes of segments of the plot using a plurality of the fluorescent values,

using the segment slopes of the plot to establish a baseline fluorescence region by generating a slope value for each of a plurality of the amplification cycles, and establishing the baseline fluorescence region comprising an interval of cycles that includes the amplification cycle with the slope value having an absolute value closest to zero, and

making the positive or negative call based on whether the fluorescence value during a selected amplification cycle is outside the baseline fluorescence region.

3. (original) The method of claim 2 wherein the baseline fluorescent region is established without the use of an internal standard.

4. (original) The method of claim 1 wherein the melting temperature analysis is performed by

obtaining a melting profile,

determining the minimum or maximum of the first derivative to generate a Tm value, and

comparing the Tm value with the known Tm of the target analyte.

5. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence between extension and denaturation during one of the amplification cycles.

6. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence between annealing and denaturation during one of the amplification cycles.

7. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence in a separate melting process subsequent to amplification.

8. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence at 0.1°C temperature increments.

9. (original) The method of claim 4 wherein the melting profile is obtained by monitoring fluorescence at temperature increments of greater than 0.1°C.

10. (original) An automated method for determining the presence of a nucleic acid comprising the steps of

placing a sample into a container containing a fluorescent entity capable of indicating the presence of the nucleic acid and capable of providing a signal related to the quantity of the nucleic acid,

placing the container into a device for amplifying the nucleic acid through a plurality of amplification cycles in the presence of the fluorescent entity,

measuring fluorescence intensity of the fluorescent entity at each of the plurality of amplification cycles to produce a fluorescent value for each cycle related to the quantity of the nucleic acid present at each cycle,

generating a plot wherein the fluorescent values are recorded for each amplification cycle,

calculating slopes of segments of the plot using a plurality of the fluorescent values,

using the segment slopes of the plot to establish a baseline fluorescence region by generating a slope value for each of a plurality of the amplification cycles, and establishing the baseline fluorescence region comprising an interval of cycles that includes the amplification cycle with the slope value having an absolute value closest to zero,

outputting a positive result if the fluorescence value of a selected amplification cycle is outside the baseline fluorescence region, and

confirming the positive result by melting temperature analysis.

11-13. (cancelled)

REMARKS

The office action mailed on November 28, 2003 required restriction of the 13 pending claims of the captioned application to one of 2 groups. The claim groups identified by the Examiner are as follows:

Group I: claims 1-10, drawn to a method of detection of nucleic acid.

Group II: claims 11-13, drawn to a PCR apparatus.

Applicant elects Group I. Claims 11-13 have been canceled.

Applicants respectfully request allowance of the pending claims and passage of the application to issuance.

Respectfully submitted,
BARNES & THORNBURG

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